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Renal Actinomycosis

With Report of a Primary Case

JAMES M. WHISENAND, M.D., and E. VINCENT MOORE, M.D.,
San Diego

PRIMARY or solitary renal actinomycosis is a rare disease. Since Israel first reported a case in 1878[8] 31 others have been recorded. Only 15 of the reported cases appear to have been truly limited to the kidney. An additional case is reported here because of the rarity of the lesion and to emphasize that recent advances in therapy demand specific identification of the actinomycete if cure is to be obtained.

ETIOLOGY

The cause of this disease is a saprophytic, facultative, anaerobic fungus. The colonies appear in the pus from lesions or are imbedded in granulation tissue and appear as irregular, yellow granules from 0.5 to 2 mm. in diameter. These are the so-called "sulfur granules." They may be soft and easily crushed or hard and calcareous. As observed microscopically, these granules have a central mass of debris, pus cells and degenerated fibers. Toward the margin is a dense network of interlacing, branched filaments. At the periphery are isolated, radiating filaments terminating in clubbed ends. The mycelial filaments are Gram-positive.

According to the classification of Weed and Bagenstoss[11] the human pathogen is called Actinomyces israeli. A. bovis is the anaerobic organism producing lumpy jaw in cattle. Nocardia is the name given the aerobic form of actinomycetes once thought to cause all cases in man and now incriminated in only 10 per cent of cases.[2, 4]

It was formerly thought that actinomycosis was contracted through ingestion or inhalation of contaminated straw, grains, or grasses, and this erroneous conception still is to be found in some present-day textbooks. It has been proved that A. israeli lives as a harmless saprophyte in the mouths, tonsils, and intestinal tracts of normal human subjects. Davis[4] stated that Naeslund cultured pure colonies of the organism from the mouths of healthy persons. These colonies, on injection, produced the disease in guinea pigs. Two cases have been reported in which actinomycosis followed human bites by persons without evidence of the disease (Cope in England and McWilliams in the United States, according to Davis).[4]

The oral cavity is the most likely portal of entry for the organism since the most common site of the disease is about the head and neck. Swallowed organisms may lodge in the cecum or appendix. Seven cases of renal actinomycosis following appendectomy have been reported. Gardiner[6] reported that 8 per cent of removed appendices contained colonies of actinomycetes.

Edwards[5] reported that Henrici was able only rarely to infect experimental animals with single injections of A. bovis. Repeated inoculations were required, suggesting that repeated exposure leading to sensitization was an etiologic factor.

Infection with other organisms may play a role in the initiation of the disease process, or in extension of it once it is present. Repeated sore throats or diseased tonsils have been noted in some patients prior to onset. Pneumonia or trauma to the chest have preceded pulmonary lesions in other instances.

PATHOLOGY

The term primary renal actinomycosis is used here in the same sense that renal tuberculosis is termed primary. That is, it must be assumed that an earlier lesion existed somewhere in the body from which the kidney became infected. The patient probably was symptomless at the time of this early lesion and demonstrable residual traces are absent. That it must have existed, however, is indicated by the presence of the disease in the kidney.

The characteristic lesions are chronic abscesses as a result of progressive penetration and destruction of tissue. Tissue reacts to the invading parasite by the formation of nodules of granulation tissue rich in vessels and cells. The centers of these nodules then break down by a process of lipoid degeneration and become filled with leukocytes, debris, and sulfur granules. In the wall of granulation tissue about the abscesses are many mononuclear and occasional giant cells. As the lesion ages, pronounced formation of connective tissue replaces most of the granulation tissue. Thus the lesion of actinomycosis is a chronic, suppurating granuloma. The lesions vary in size from that of a pinhead to that of a grapefruit.

Extension from the primary site is usually by direct spread to tissue and along fascial planes. The lymphatic system is almost immune and the lymph nodes do not react and enlarge. The skin is involved late in the process, as it offers great resistance. Muscles and nerves may be invaded or pushed aside. Bones may be superficially involved by direct continuity. Rarely, hematogenous spread occurs and then any organ may be involved. Primary renal actinomycosis is initiated in this manner. Secondary renal lesions occur when the kidney is involved contiguously.

Grossly, a variety of pathologic changes may be observed in the infected kidney. When the lesion is minimal, only one small area is affected. On cut surface of the kidney a pyramidal area of granulation and scar tissue may be observed, the apex pointing toward the renal pelvis in the region of a renal papilla indicating the hematogenous origin of the infection. Within this may be seen yellowish streaks or granules, and abscess cavities of varying size which may also contain the yellow sulfur granules. The granuloma may extend through the capsule to invade the perinephric fat. Frequently a perirenal abscess is produced. When involvement is more diffuse, the entire kidney may be converted into a suppurating, granulomatous mass. Subsequently, multiple sinus tracts discharge to the skin. If the involvement begins in the lower pole and spreads to include and obstruct the

From the Department of Urology, San Diego County General Hospital.

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ureter, hydronephrosis will appear. Calculus formation and pyonephrosis are logical sequelae. Such calculi may be composed of a fossilized mass of actinomycetes, as in Israel's case, in which, presumably, a parasitic colony served as the nucleus for the deposition of urinary salts.

Unlike renal tuberculosis, in which predilection for involvement of the ureter and the bladder is so common, in actinomycosis apparently the infected urine may be discharged from an actinomycotic kidney for weeks or even months without producing any pathologic changes in the urinary passages below.[6]

DIAGNOSIS

In a review of 33 cases—16 in which renal actinomycosis was solitary (demonstrable only in the kidney) and 17 in which it was confined mainly to the kidney—it was noted that the commonest symptoms and signs reported resembled those of renal tuberculosis, pyogenic infection or tumor. The symptoms and signs in the order of frequency are listed in Table 1.

The disease was correctly diagnosed in eight cases before operation or autopsy. The organisms were found in the urine in five cases, in pus from draining sinuses in two, and in both urine and pus in one case.

Renal tumor was diagnosed in nine cases, renal tuberculosis in five, and renal infection in six. Ureteral calculus was the preliminary diagnosis and finding in three cases. Perinephric abscess was the primary diagnosis in two cases and was an associated development in nine others. Spontaneously draining sinuses were noted in one patient. Sinuses occurred after incision and drainage of a perinephric abscess or exploration in eight cases, and after nephrectomy in seven.

Cystoscopy may demonstrate nothing abnormal or only the changes of inflammation. Gardiner[6] observed sulfur granules on the vesical mucosa about the ureteral orifices in one case.

Pyelograms may disclose the typical deformity of a renal tumor, the moth-eaten ulceration of tuberculosis, the changes of chronic infection, or the signs associated with perinephric abscess. Ureteral involvement may also simulate the irregular moth-eaten appearance of tuberculosis. Gardiner reported shortening of the ureter with obliteration of its pelvic curve.

TREATMENT

Treatment of actinomycosis when confined to the kidney has been much more satisfactory than treatment of abdominal actinomycosis. Comprising only 20 per cent of all cases, abdominal actinomycosis has accounted for over 50 per cent of the deaths. In Davis' series all patients died within 14 months.[4]

Nephrectomy was done in 22 of the 33 cases reviewed by the author. Six of the patients died within one year and the others recovered. Reports of progress, however, were far from complete. Of the 16 patients with solitary renal actinomycosis, 13 were treated by nephrectomy and two died.

Experience with the sulfonamides and the antibiotics has brought some encouraging results, but these methods of therapy are specific and demand specific and accurate diagnosis.[1, 2, 3, 11, 12] Actinomyces israeli and A. bovis respond to penicillin but not to sulfonamides. The reverse is true of the aerobic form, Nocardia asteroides, which causes 10 per cent of the infections in man. Treatment with sulfonamides and penicillin is not to be undertaken lightly in this disease because of the large amounts sometimes required. In one case of abdominal actinomycosis recently reported, 30 to 40 million units of penicillin was given daily for eight days, 11 to 14 million units daily for 26 days, and 800,000 units daily for 29 days. Cure was achieved after an illness of 16 months in which treatment consisted in the usual doses of penicillin.[10] In a case reported by Glover[7] in 1948 a patient with a pulmonary infection with the Nocardia organism received 1,268 gm. of sulfadiazine in a five-month period.

TABLE 1.—*Incidence of Signs and Symptoms of Renal Actinomycosis as Reported in 33 Cases in the Literature*

	Number of Times Reported
Specific Symptoms:	
Pain in the flank	22
Mass in the flank or abdomen	14
Chills and fever	14
Irritative vesical symptoms	11
Draining sinuses	10
Hematuria	8
Pyuria	4
General Symptoms:	
Malaise	14
Loss of weight	13
Low grade fever	10
Anemia	9

Streptomycin does not appear to offer much promise in the therapy of actinomycosis. Resistant strains develop quickly.[3] Reports of treatment with aureomycin or chloromycetin have not reached the literature yet.

Weed and Bagenstoss[12] recently emphasized some of the problems in making an accurate diagnosis. They stated that it is frequently impossible to make an etiologic diagnosis from histologic study alone as has been done in the majority of the reported cases. A wide variety of other organisms not sensitive to the sulfonamides or to penicillin may produce granules resembling those of actinomycosis. To differentiate them, a Gram stain of the section of tissue must be done and the filaments typical of actinomycosis demonstrated. Even after these filaments are found, the anaerobic (A. israeli) and the aerobic (N. asteroides) forms remain to be differentiated. However, most of the aerobic forms are acid-fast and identification thus can be made by use of the Ziehl-Nielsen stain. Accurate diagnosis and choice of specific therapy depend upon accurate bacteriologic study.

The fundamental surgical principles of adequate drainage and excision of devitalized tissue should be followed. No amount of chemotherapy will avail if these are ignored.

Iodides, methenamine, x-ray and radium and diverse vaccines[9] have all been used in the past without much success.

REPORT OF A CASE

A 77-year-old white woman was admitted to the San Diego County General Hospital June 18, 1949, complaining of inability to urinate for two days and irritative symptoms, referable to the bladder, of increasing severity for several weeks. The patient was confused, irrational, and obviously critically ill. The patient had been under the care of two different urologists during the previous two years and had been treated for chronic, recurrently acute urinary infection.

The patient had been well until two and a half years before admission when she began to have increasingly severe irritative and obstructive vesical symptoms. A complete urologic survey two years prior to admission had disclosed a prominent cystocele, a bar type of obstruction at the vesical neck, acute cystitis, acute right pyelonephritis, a calculus 5 mm. in diameter in the low major calyx of the right kidney, and grade I, right-sided, congenital hydronephrosis with slight caliectasis. The left kidney was essentially normal (Figure 1, *left*). The vesical urine contained many pus cells and Gram-negative bacilli. Additional findings were auricular fibrillation and electrocardiographic evidence of chronic coronary insufficiency. There was slight residual evidence of a recent, mild cerebrovascular accident. Perineorrhaphy was done shortly thereafter.

The symptoms and infection of the urinary tract persisted, leading to another urologic survey several months later. New findings at that time included severe ulcerative cystitis and a patulous right ureteral orifice. Retrograde pyelograms showed "nephroptosis on the right with chronic caliectasis, pyelectasis, and hydro-ureter. The upper one-third of the right ureter was displaced to the midline." No pronounced changes were noted in the left kidney (Figure 1, *right*). Cultures of the vesical and renal urine produced E. coli. Numerous courses of sulfonamides, penicillin, and one of streptomycin were administered, and while all controlled the acute exacerbations of the infection, they did not eliminate the pyuria.

This conservative therapy resulted in some amelioration of the irritative symptoms referable to the bladder, but the patient went into a slowly progressive decline and was referred to the San Diego County Hospital. On admission, an ovoid, smooth, firm, movable, non-tender mass, 10 by 15 cm., was palpable in the region of the right kidney. The blood pressure was 150 mm. of mercury systolic and 90 diastolic. The temperature was 100° F. On catheterization of the bladder 75 cc. of purulent urine was obtained. Thereafter urinary output varied from one to two liters daily. The urine contained many pus cells and Gram-negative bacilli. Erythrocytes numbered 3,220,000 per cu. mm. of blood, and hemoglobin value was 58 per cent. Leukocytes numbered 17,950 with 89 per cent polymorphonoclear leukocytes and 10 per cent lymphocytes. The urea nitrogen content of the blood was 12.3 mg. per 100 cc.

Generalized acute cystitis, trigonal hypertrophy and inflamed, edematous ureteral orifices were noted in cystoscopic examination. The vesical urine contained 10 to 12 pus cells per high power field, and Gram-negative rods and Gram-positive diplococci. In urine from the kidneys there was

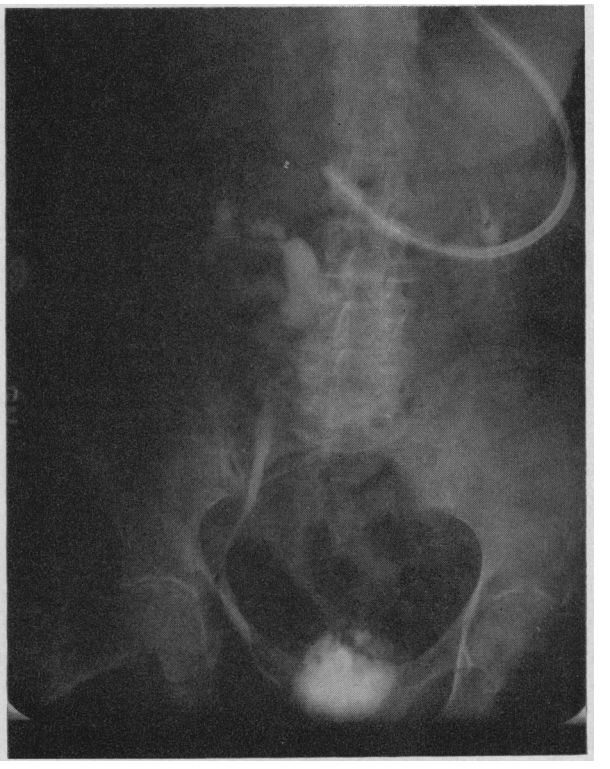

Figure 2.—Retrograde pyelogram at time of admission of patient to hospital, illustrating expanding lesion of the lower pole of the right kidney displacing the pelvis and upper part of the ureter medially and compressing and distorting the lower calyces.

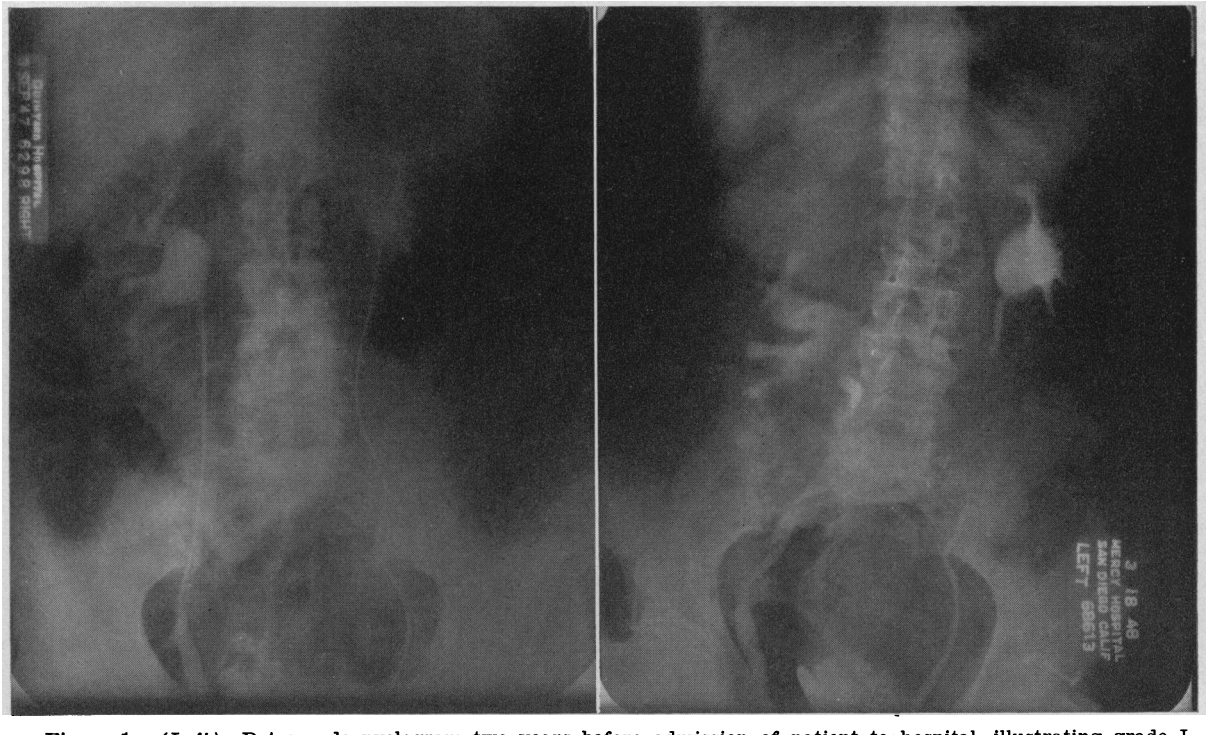

Figure 1.—*(Left):* Retrograde pyelogram two years before admission of patient to hospital, illustrating grade I, right-sided, congenital type hydronephrosis with slight caliectasis. A calculus 5 mm. in diameter was noted in the right lower major calyx on plain films. *(Right):* Retrograde pyelogram one year before admission, illustrating increase in the right-sided hydronephrosis and displacement medially of the upper part of the ureter on the right side. Grade I nephroptosis also has appeared.

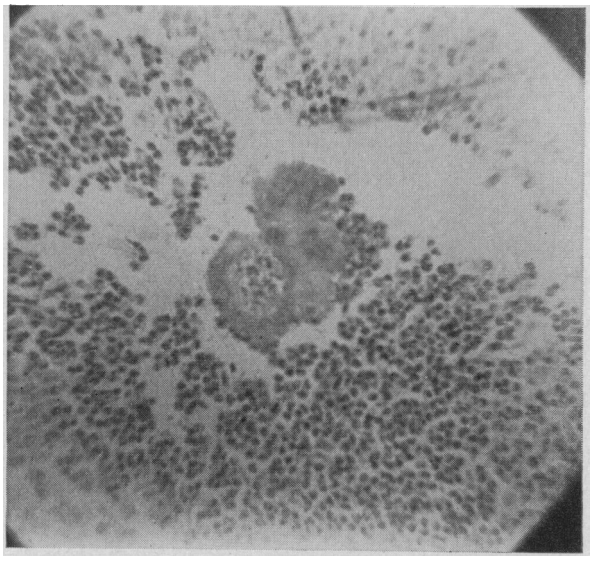

Figure 3.—Photomicrograph of an actinomycotic colony in one of the small abscesses in the granulomatous tumor of the right kidney.

an occasional pus cell but no bacteria. The excretion of phenolphthalein was normal on the left side but decreased on the right, the dye not appearing for eight minutes and only 2.5 per cent being obtained in ten minutes. Retrograde pyelograms showed no change from previous films on the left side. On the right side, an expanding lesion of the lower pole of the kidney displacing the pelvis and upper ureter medially and compressing and distorting the lower calyces, was observed (Figure 2). The diagnosis was tumor of the right kidney. However, operative intervention was not proposed in view of the obvious terminal condition of the patient.

Despite penicillin and sulfadiazine, a "septic" temperature curve persisted, although the pyuria cleared. The hospital course was progressively downhill and the patient died 12 days after admission.

At autopsy a granulomatous tumor was found to occupy the lower pole of the right kidney, most of which had been destroyed. The granulomatous process involved the perinephric fat adjacent to it. No large collection of pus was found. The pelvis and calyces were not invaded. Grossly the lesion resembled actinomycosis and this diagnosis was substantiated by histologic study (Figure 3). No other actinomycotic foci were found.

SUMMARY

Reported in this presentation is a case of primary renal actinomycosis simulating tumor. It is believed to be the sixteenth case of record in which the disease was confined to the kidney.

Since specific chemotherapy (combined with surgical treatment) recently has given encouraging results in the management of actinomycosis, accurate and specific diagnosis is essential, first to establish the presence of actinomyces, and then to determine the particular strain of the fungus so that the most effective sulfonamide or antibiotic agent may be selected. This may be accomplished through adequate bacteriologic studies.

3415 Sixth Avenue.

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